

22. (Amended) A compound according to claim 1 wherein

R^1 is selected from the group consisting of hydrogen, halogen and haloalkyl,

R^2 is selected from the group consisting of hydrogen and halogen,

R^3 is a pyrimidine, and

R^4 and R^5 are each hydrogen.

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23. (Amended) A compound according to claim 22 wherein

R^1 is trifluoromethyl,

R^2 is hydrogen, and

R^3 is a pyrimidine.

24. (Amended) A compound according to claim 22 wherein R^1 and R^2 are each chloro, and R^3 is a pyrimidine.

REMARKS

I. Status of the Claims

Claims 1-27 are pending in the application. Claims 1-3, 5, 7, 12, 14, 17-20, and 22-24 have been amended. Claim 15 is withdrawn from consideration.

Claims 3, 12, 14, and 20 have been amended to correct typographical errors.

Claims 3 and 12 have been amended to replace " $p(R^{12})$ " with " $(R^{12})_p$." Claims 14 and 20 have been amended to replace " R_{10} " and " R_{11} " with " R^{10} " and " R^{11} ," respectively, as the superscripted labels have antecedent basis in claim 1.

The other claim amendments are discussed with respect to the claim objection and § 112, second paragraph rejections, below.

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No new matter has been added by these amendments, nor do these amendments raise new issues or necessitate the undertaking of any additional search of the art by the Examiner. Accordingly, Applicants respectfully request reexamination of the claims.

II. Objection to the claims

The Examiner has objected to the claims as allegedly "drawn to multiple inventions for reasons set forth in the restriction requirement." *Office Action* at p. 3.

Applicants have amended claims 1, 2, 5, 7, 14, 17-20, and 22-24 to conform with their election in response to the restriction requirement. Specifically, claim 1 has been amended to recite "wherein at least one of R¹ or R³ is a pyrimidine." Claims 2, 5, 7, 14, 17-20, and 22-24 have been amended to specify that either R¹ or R³ is a pyrimidine.

Applicants have also amended Claim 7, consistent with their election in response to the restriction requirement, to incorporate the pyrimidine-containing compounds disclosed in the specification. Specifically, claim 7 now recites, in addition, 4-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-morpholine (example 13), 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidin-4-ol (example 14), 4-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-2,5-dimethyl-morpholine (example 15), 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid amide (example 16), 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-4-carboxylic acid amide (example 17), N-Ethyl-N-1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-pyrrolidin-3-yl)-

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acetamide (example 18), 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid ethyl ester (example 19), 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-4-carboxylic acid ethyl ester (example 20), 4-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperazine-1-carboxylic acid ethyl ester (example 21), 4-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperazin-1-yl-acetic acid ethyl ester (example 22), (3-imidazol-1-yl-propyl)-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-amine (example 23), 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-4-carboxylic acid (example 24), 4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid (example 26), 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid diethyl amide (example 27), N-1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-pyrrolidin-3-yl)-acetamide (example 32), 4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-6-(2-methoxymethyl-pyrrolidin-1-yl)-pyrimidine (example 33), 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-pyrrolidin-3-ol (example 34), (1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-pyrrolidin-3-yl)-carbamic acid *tert*-butyl ester (example 35), isopropyl-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-methyl amine (example 36), and ethyl-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-methyl-amine (example 37).

Accordingly, it is respectfully requested that the objection to the claims be withdrawn.

III. Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-14 and 16-27 stand rejected under 35 U.S.C. § 112, second paragraph for indefiniteness. Applicants respectfully traverse this rejection.

Claim 1 is rejected "because the dotted lines in formula II are not clear." *Office Action* at p. 4. Applicants submit that one of ordinary skill in the art would readily understand that the dotted lines represent optional bonds depending on the particular substituents D, B, Y and Z, *i.e.*, the dotted line indicates that the formula contains a single or double bond. According to claim 1, D, B, Y and Z can be a group such as -O- or -N=. For example, where D, B, Y or Z is -O-, then D, B, Y or Z contains only single bonds; where D, B, Y or Z is -N=, then the dotted line signifies a bond and D, B, Y or Z has a double bond.

Definiteness under 35 U.S.C. § 112, second paragraph is determined from the point of view of one of ordinary skill in the art. M.P.E.P. § 2173.02. ("[T]he examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope."). Because one of ordinary skill in the art would readily understand that the dotted line indicates an optional bond, Applicants respectfully submit that claim 1 satisfies § 112, second paragraph.

The Examiner also rejects claim 1, alleging that "heterocyclyl" is indefinite. Although Applicants disagree that "heterocyclyl" is indefinite from the point of view of one of ordinary skill in the art, to expedite prosecution, claim 1 has been amended to further define heterocyclyl by ring size, heteroatoms, and optional groups. Support for this amendment can be found in the specification at p. 6, line 5 to p. 7, line 9.

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Claims 1-27 are rejected because "there is a vertical line on the right hand side of every page ... overlapping with the claims." Applicants believe this line was the result of a faulty facsimile reproduction. Applicants enclose a clean copy of the Response and Amendment filed on August 23, 2002.

Claim 14 is rejected for lacking a period. Claim 14 has been amended by adding the period. Claim 20 has also been amended by inserting a period.

By these amendments and remarks, Applicants respectfully submit that the claims now satisfy 35 U.S.C. § 112, second paragraph. Accordingly, Applicants respectfully request withdrawal of the rejection.

IV. Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims. If the Examiner believes a telephone conference would be useful in resolving any outstanding issues, he is invited to call the undersigned at (617) 452-1621.

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Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
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By: *Maria Bautista*
Maria T. Bautista
Reg. No. 52,516

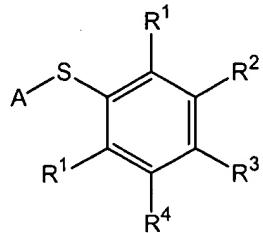
Date: July 15, 2003

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APPENDIX: MARKED-UP COPY OF CLAIM AMENDMENTS

1. (Twice Amended) A compound of formula I

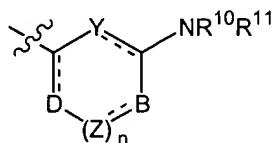


I

or a pharmaceutically acceptable salt or prodrug thereof,

wherein at least one of R¹[,] or R³ is a pyrimidine;

R², [R³], R⁴ and R⁵ are each independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, cyano, nitro, cycloalkyl, carboxaldehyde, and a group of formula II defined as



II

subject to the proviso that one or more than one of R¹ or R³ is a group of formula II as defined above;

wherein D, B, Y and Z at each occurrence are independently selected from the group consisting of -CR⁶=, -CR⁷R⁸-, -C(O)-, -O-, -SO₂-, -S-, -N=, and -NR⁹-;

n is an integer of zero to three;

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R^6 , R^7 , R^8 and R^9 , at each occurrence, are each independently selected from the group consisting of hydrogen, alkyl, carboxy, hydroxyalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl and carboxyalkyl; and R^{10} and R^{11} are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkoxyalkyl, alkoxycarbonylalkyl, carboxyalkyl, hydroxyalkyl, heterocycl, heterocyclalkyl and heterocyclamino; or R^{10} and R^{11} are taken together with N to form a three to seven membered unsubstituted heterocycl ring, or a three to seven membered substituted heterocycl ring, substituted with one or more than one substituent R^{13} , wherein R^{13} , at each occurrence is independently selected from the group consisting of alkyl, alkylene, alkoxy, alkoxyalkyl, cycloalkyl, aryl, heterocycl, heterocyclalkyl, heterocyclcarbonyl, heterocyclalkylaminocarbonyl, hydroxy, hydroxyalkyl, hydroxyalkoxyalkyl, carboxy, carboxyalkyl, carboxycarbonyl, carboxaldehyde, alkoxycarbonyl, arylalkoxycarbonyl, aminoalkyl, aminoalkanoyl, aminocarbonyl, carboxamido, alkoxycarbonylalkyl, carboxamidoalkyl, cyano, tetrazolyl, alkanoyl, hydroxykanoyl, alkanoyloxy, alkanoylamino, alkanoyloxyalkyl, alkanoylaminoalkyl, sulfonate, alkylsulfonyl, alkylsulfonylaminocarbonyl, arylsulfonylaminocarbonyl and heterocyclsulfonylaminocarbonyl; wherein A is an unsubstituted aryl group, an unsubstituted heterocycl group, a substituted aryl group, or a substituted heterocycl group, substituted with one or more than one substituent R^{12} , wherein R^{12} , at each occurrence, is

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independently selected from the group consisting of halogen, alkyl, aryl, haloalkyl, hydroxy, alkoxy, alkoxyalkyl, alkoxy carbonyl, alkoxyalkoxy, hydroxyalkyl, aminoalkyl, aminocarbonyl, alkyl(alkoxycarbonylalkyl) aminoalkyl, heterocyclyl, heterocyclylalkyl, carboxaldehyde, carboxaldehyde hydrazone, carboxamido, alkoxy carbonylalkyl, carboxy, carboxyalkyl, carboxyalkoxy, hydroxyalkylaminocarbonyl, cyano, amino, heterocyclylalkylamino, carboxythioalkoxy, carboxycycloalkoxy, thioalkoxy, carboxyalkylamino, trans-cinnamyl and heterocyclylalkylaminocarbonyl; and

wherein R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹² and R¹³ are unsubstituted or substituted with one or more than one electron donating or electron withdrawing group

wherein the heterocyclyl is chosen from 4-, 5-, 6- and 7-membered rings

containing 1-3 heteroatoms independently selected from nitrogen, oxygen and sulfur; the 4- and 5-membered rings have zero to two double bonds and the 6- and 7-membered rings have zero to three double bonds, the heterocycle being optionally substituted with alkyl, halogen, hydroxy or alkoxy substituents,

further wherein the heterocyclyl optionally comprises a group chosen

from:

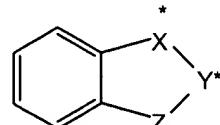
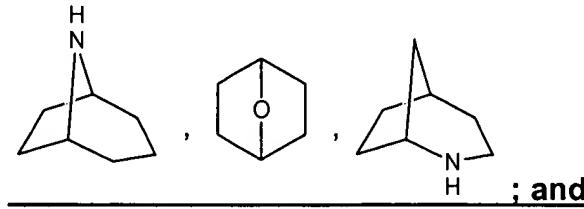
(i) bicyclic, tricyclic and tetracyclic groups in which any of the above heterocyclic rings is fused to one or two rings independently selected from an aryl ring, a cyclohexane ring, a cyclohexene

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ring, a cyclopentane ring, a cyclopentene ring, and another monocyclic heterocyclic ring;

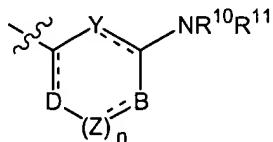
(ii) bridged bicyclic groups where a monocyclic heterocyclic group is bridged by an alkylene group optionally selected from



(iii) compounds of the formula

independently selected from $-\text{CH}_2-$, $-\text{CH}_2\text{NH}-$, $-\text{CH}_2\text{O}-$, $-\text{NH}-$ and $-\text{O}-$, with the proviso that at least one of X^* and Z^* is not $-\text{CH}_2-$, and Y^* is selected from $-\text{C}(\text{O})-$ and $-(\text{C}(\text{R}'')_2)_v-$, where R'' is hydrogen or alkyl of one to four carbons, and v is 1-3.

2. (Twice Amended) A compound according to claim 1 wherein R^3 is the group of formula II



II

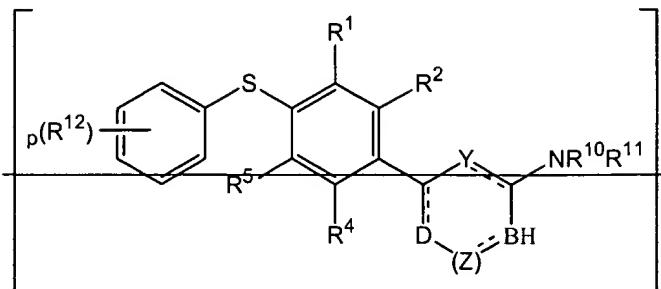
wherein R^{10} , R^{11} , D , B , Y , Z , and n are defined as in claim 1; and

R^1 is defined as in claim 1 with the proviso that if R^3 does not define a pyrimidine, then R^1 is a pyrimidine.

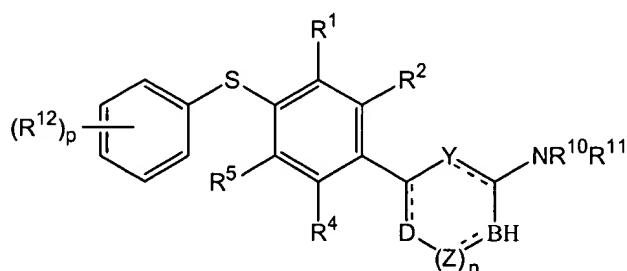
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3. (Twice Amended) A compound according to claim 1 of formula III



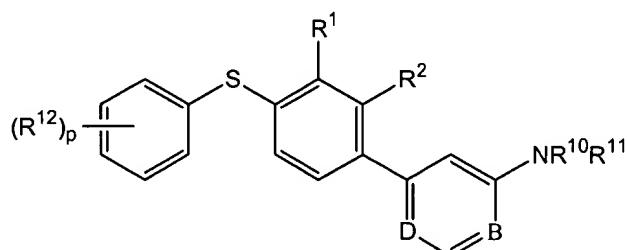
III



III

wherein R¹, R², R⁴, R⁵, R¹⁰, R¹¹, R¹², D, B, Y, Z, and n are defined as in claim 1;
and p is an integer of zero to five.

5. (Twice Amended) A compound according to claim 1 of formula IV



IV

wherein D and B are each independently selected from the group consisting of
-N= and -CR⁶=;

R^1 is selected from the group consisting of hydrogen, halogen and haloalkyl, with the proviso that if R^3 does not define a pyrimidine, then R^1 is a pyrimidine;

~~[R¹ and] R² [are each independently]~~ is selected from the group consisting of hydrogen, halogen and haloalkyl;

R^{10} and R^{11} are defined as in claim 1;

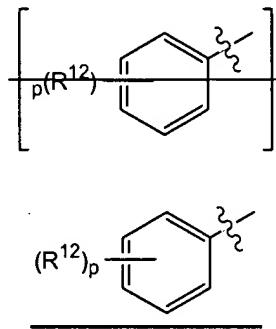
R^{12} , at each occurrence, is independently selected from the group consisting of halogen, alkyl, haloalkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclyl, wherein R^{12} is unsubstituted or substituted with at least one electron donating group or electron withdrawing group; and

p is an integer of zero to five.

~~pyrrolidine-3-yl) acetamide, N-1-(4-(4-(2-methoxy-phenylsulfanyl)-3-trifluoromethyl-phenyl) pyridin-2-yl) pyrrolidine-3-yl) acetamide, N-1-(4-(4-(2-methoxy-phenylsulfanyl)-3-trifluoromethyl-phenyl) pyridin-2-yl) pyrrolidine-3-yl) acetamide, 4'-(4-(2,3-dihydro-benzo(1,4)dioxin-6-ylsulfanyl)-3-trifluoromethyl-phenyl)-3,4,5,6-tetrahydro-2H-(1,2')bipyridinyl-4-carboxylic acid, and 4'-(4-(2,3-dihydro-benzo(1,4)dioxin-6-ylsulfanyl)-3-trifluoromethyl-phenyl)-3,4,5,6-tetrahydro-2H-(1,2')bipyridinyl-3-carboxylic acid] 4-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-morpholine, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidin-4-ol, 4-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-2,5-dimethyl-morpholine, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid amide, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-4-carboxylic acid amide, N-Ethyl-N-1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-pyrrolidin-3-yl)-acetamide, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid ethyl ester, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-4-carboxylic acid ethyl ester, 4-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperazine-1-carboxylic acid ethyl ester, 4-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperazin-1-yl-acetic acid ethyl ester, (3-imidazol-1-yl-propyl)-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-amine, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-4-carboxylic~~

acid, 4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-piperidine-3-carboxylic acid diethyl amide, N-1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-pyrrolidin-3-yl)-acetamide, 4-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-6-(2-methoxymethyl-pyrrolidin-1-yl)-pyrimidine, 1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-pyrrolidin-3-ol, (1-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-pyrrolidin-3-yl)-carbamic acid *tert*-butyl ester, isopropyl-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-methyl amine, and ethyl-(6-(4-(2-isopropyl-phenylsulfanyl)-3-trifluoromethyl-phenyl)-pyrimidin-4-yl)-methyl-amine.

12. (Amended) A compound according to claim 1 wherein A is an unsubstituted or substituted aryl group of the formula

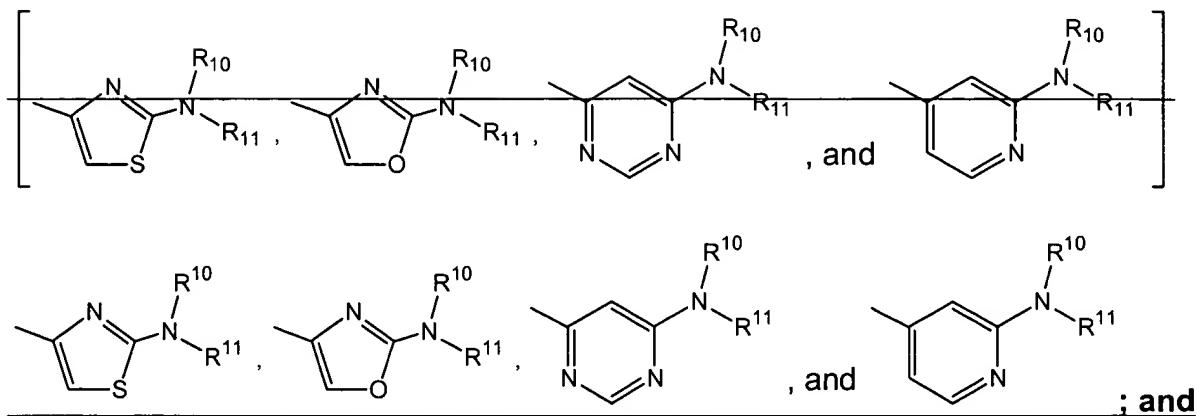


wherein R¹² is defined as in claim 1; and p is an integer of 0 to 5.

14. (Amended) A compound according to claim 1 wherein R³ is selected from the group consisting of

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R¹ is defined as in claim 1 with the proviso that if R³ does not define a pyrimidine, then R¹ is a pyrimidine.

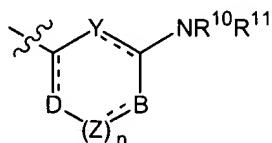
17. (Amended) A compound according to claim 1 wherein

R¹ is selected from the group consisting of hydrogen, halogen, alkyl and nitro, with the proviso that if R³ does not define a pyrimidine, then R¹ is a pyrimidine;

[R¹ and] R² [are each independently] is selected from the group consisting of hydrogen, halogen, alkyl, and nitro;

R⁴ and R⁵ are each independently selected from the group consisting of hydrogen and alkyl; and

R³ is



wherein

D is -CR⁶= or -N=,

B is -S-, -O-, -CR⁶= or -N=,

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Y is $-\text{CR}^6=$ or $-\text{N}=$,

Z is $-\text{CR}^6=$ or $-\text{N}=$; and

n is zero or one

18. (Amended) A compound according to claim 1 wherein

R^1 and R^2 are each independently selected from the group consisting of hydrogen, halogen, and haloalkyl; [and]

R^3 is a pyrimidine; and

R^4 and R^5 are each independently hydrogen.

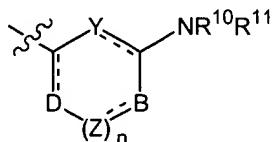
19. (Amended) A compound according to claim 1 wherein

R^1 is selected from the group consisting of hydrogen, halogen and haloalkyl, with the proviso that if R^3 does not define a pyrimidine, then R^1 is a pyrimidine;

$[\text{R}^1$ and] R^2 [are each independently] is selected from the group consisting of hydrogen, halogen, and haloalkyl;

R^4 and R^5 are each independently hydrogen; and

R^3 is



wherein

D is $-\text{CR}^6=$ or $-\text{N}=$,

B is $-\text{S}-$, $-\text{O}-$, $-\text{CR}^6=$ or $-\text{N}=$,

Y is $-\text{CR}^6=$ or $-\text{N}=$,

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Z is $-CR^6=$ or $-N=$; and

n is zero or one.

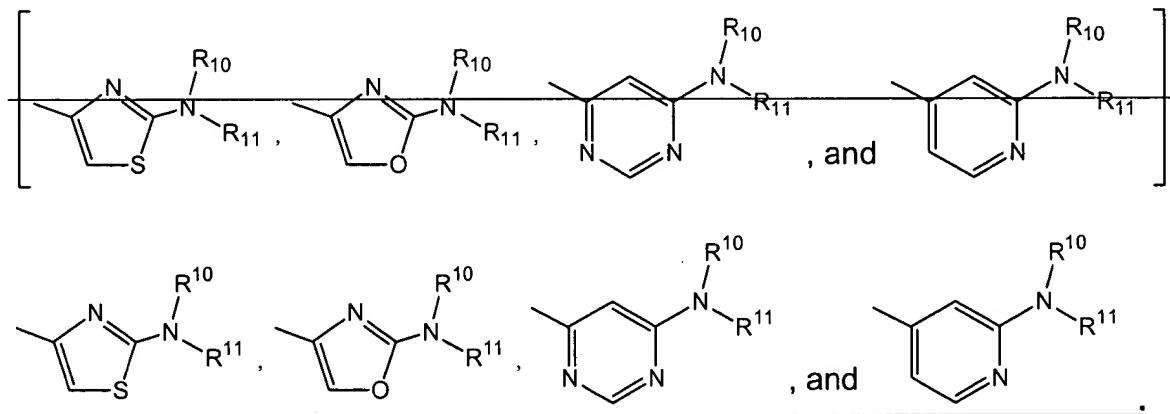
20. (Amended) A compound according to claim 1 wherein

R^1 is selected from the group consisting of hydrogen, halogen and haloalkyl, with the proviso that if R^3 does not define a pyrimidine, then R^1 is a pyrimidine;

$[R^4$ and] R^2 [are each independently] is selected from the group consisting of hydrogen, chloro, and trifluoromethyl;

R^4 and R^5 are each independently hydrogen; and

R^3 is selected from the group consisting of



22. (Amended) A compound according to claim 1 wherein

R^1 is selected from the group consisting of hydrogen, halogen and haloalkyl,

R^2 is selected from the group consisting of hydrogen and halogen, [and]

R^3 is a pyrimidine, and

R^4 and R^5 are each [independently] hydrogen.

23. (Amended) A compound according to claim 22 wherein

R^1 is trifluoromethyl, [and]

R^2 is hydrogen, and

R^3 is a pyrimidine.

24. (Amended) A compound according to claim 22 wherein R^1 and R^2 are each
[independently] chloro, and R^3 is a pyrimidine.

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